DIGITALCOMMONS @WAYNESTATE

Clinical Research in Practice: The Journal of Team Hippocrates

Volume 1 | Issue 1 Article 5

2015

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Recommended Citation

Provenzano AM. MRI is the most effective initial diagnostic study for osteomyelitis of the foot in diabetic patients. *Clin. Res. Pract.* 2015;1(1):eP1000. doi: 10.22237/crp/1422568065

Clinical Research in Practice
The Journal of Team Hippocrates
VOL 1 ISS 1 / eP1000 / JANUARY 2015

META-ANALYSIS REVIEW:

MRI is the most effective initial diagnostic study for osteomyelitis of the foot in diabetic patients

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ABSTRACT What is the best initial diagnostic study that should be used for a suspected osteomyelitis diagnosis? A critical review and clinical application of: Kapoor A, Page S, LaValley M, Gale DR, Felson DT. Magnetic resonance imaging for diagnosing foot osteomyelitis: a meta-analysis. *Arch Intern Med.* 2007;167(2):125-132. doi:10.1001/archinte.167.2.125. ***Keywords***: foot osteomyelitis, MRI, magnetic resonance imaging, diabetes, diagnostic methods, Charcot joint

Clinical Context

During our infectious disease rounds, we had a patient with suspected osteomyelitis due to a painful toe joint with overriding necrotic ulceration; the patient also had diabetes as comorbidity. Our attending decided to order an MRI (magnetic resonance imaging) as the initial study to work up the possible osteomyelitis. This confused me because at other clerkship sites, we had done bone scans as the initial diagnostic work-up for osteomyelitis.

Clinical Question

What is the best initial diagnostic study that should be used for a suspected osteomyelitis diagnosis?

Research Article

Kapoor A, Page S, LaValley M, Gale DR, Felson DT. Magnetic resonance imaging for diagnosing foot osteomyelitis: a meta-analysis. *Arch Intern Med.* 2007;167(2):125-132. doi:10.1001/archinte.167.2.125.

Literature Review

The above-identified research article, provided by a mentor, examined the four most widely used diagnostic tests for osteomyelitis. Keywords derived from this meta-analysis led to multiple prospective trials relevant to the topic of osteomyelitis diagnosis in diabetic patients using MRI. All of the studies included[1-38] had small sample sizes (the largest was only 72)[1], and many were not designed prospectively nor were they randomized. This meta-analysis has been cited in multiple articles referring to osteomyelitis and is often used as the benchmark study for this subject. This makes it the most relevant article related to imaging techniques in the setting of potential osteomyelitis. Within the meta-analysis, the studies were chosen with the following selection criteria: "Studies were en-rolled when information from the usual diagnostic performance 2x2 table… could be extracted about discrete foot and ankle cases, when 80% or more of the patients were 16 years or older, and when at least one site with the disease and one without were identified by the reference standard." There were 2,053 potential studies excluded from the meta-analysis because

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they were unable to meet the criteria mentioned above, or because a patient was reused in two studies. One study was also excluded that included a Charcot joint; this is important because in the article, the authors explain that MRI changes seen in osteomyelitis can be confused when a Charcot joint is present. This is an area of potential selection bias, which will be examined in detail later.

Critical Appraisal

This meta-analysis provides level 2a evidence using the Oxford and National Guidelines Clearinghouse criteria, because it provides data from cohort and randomized controlled trials. One of the advantages of this study is that it provides a cut-off point for the sensitivity of MRI, which is clinically relevant at 90%. It also provides receiver operator curves with relevant cut points and scales showing the area under curve (AUC) of MRI against the AUC of the three other tests. This kind of direct comparison makes it easy to see the global evidence and superiority of MRI graphically. The drawback of this technique is that it cannot determine the strengths and weaknesses of each individual data set, because it works as an average. A likelihood ratio matrix showing the strengths and weak-nesses of each individual study could strengthen this meta-analysis. Instead, the study uses diagnostic odds ratios, thus providing good evidence that the MRI is the best imaging technique to diagnose osteomyelitis of the foot and ankle in adults. Even in subsets that included different designs and more diverse patients, the superior performance of MRI remained statistically relevant. However, there are many flaws in this meta-analysis. For example, very few of the studies used in the meta-analysis followed up the MRI, and corroborated the evidence of osteomyelitis, with the gold standard of biopsy; thus, the comparison of MRI against other techniques for diagnosis was not entirely complete. Also, as noted earlier, the exclusion of documentation regarding Charcot foot is a potential confounding variable since this is often confused with osteomyelitis on MRI. It would be good to establish a best initial diagnostic procedure in this subset of patients.

The largest and most relevant study within this meta-analysis is by Ledermann et al.[1], which uses standard primary signs (the presence of focally decreased marrow signal on T1 weighted images, and increased marrow signal on T2 weighted images), as well as many secondary signs like ulcers or cortical disruption, on MRI to determine a positive result. The positive likelihood ratio of this study is 5.62 and the negative likelihood ratio is 0.112. These numbers mean that when MRI is positive there is a moderate increase in the likelihood of having osteomyelitis, and when MRI is negative there is moderate-strong decrease in the likelihood of disease.[38] These data agree with the claim put forth in the meta-analysis.

Clinical Application

After reading this study, it makes sense that we ordered an MRI for my patient because it provides the best initial imaging to diagnose osteomyelitis. Before the MRI results were available, the patient was started on empiric antibiotics. Making a correct diagnosis is essential to avoid continuing antibiotics, which have potentially serious side effects if the patient does not have osteomyelitis. For this patient, the MRI was positive and was confirmed by bone biopsy done for culture and identification of the organism.

Three learning points to share:

1.) I learned that bone scans are inferior to MRI for diagnosing osteomyelitis because of excess false positive and false negative results.

2.) For my future career, I learned that I would not prescribe antibiotics to patients suspected of having osteomyelitis but who are clinically stable until the MRI results are available.

3.) I want to share with my peers that different consultants can give conflicting advice and that ultimately, we as the provider need the ability to make judgment calls regarding appropriate treatment and evaluation plans.

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